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EDITOR'S PAGE

On the Selling of Pharmaceuticals

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While growing up I worked in my father's fruit and vegetable store, went with him to buy produce at the local farmer's market, and helped him sell Christmas trees and flowers at Easter. I was thereby afforded a rich experience in the process of negotiating price and selling goods in the marketplace. It rapidly became apparent that the price for many items depended on how they were marketed and what someone could be convinced to pay for them. For some reason, it seemed that this characteristic did not apply to pharmaceuticals. Recently, however, several instances of marketing and selling of prescription drugs have demonstrated that the same principles do seem to apply.

The first example of the differential pricing of pharmaceuticals that I became aware of related to the drug finasteride, which was marketed as Proscar to treat prostatic hypertrophy. After its introduction, it became clear that the agent was also capable of inducing hair growth, and it was approved as Propecia to treat baldness. However, the price for the agent varied considerably for the two indications. Our local pharmacies currently chart $2.00 out of pocket for a 1-mg pill of Propecia but $3.00 for a 5-mg Proscar pill. Obviously, breaking the 5-mg Proscar in even quarters would reduce the cost to $0.75. Because Propecia could be considered a discretionary "quality-of-life" drug, the price differential did not make much of an impression.

A similar example of variable pricing has recently occurred with sildenafil. When sold for erectile dysfunction as Viagra, a 50-mg pill costs about $1.15; when sold as Revatio to treat pulmonary hypertension, a 20-mg pill costs about the same. Splitting a 50-mg Viagra in two would half the price of the agent for a patient for whom Revatio is prescribed. This could be especially significant because Revatio is to be taken three times per day. Of course, the number of patients with pulmonary hypertension is presumably much less than those with erectile dysfunction.

The foregoing situations were brought into focus by the recent approval of BiDil. This drug is the first to be approved for a specific race, and it raises a number of medical as well as financial issues. As is well known, BiDil is a combination of hydralazine and isosorbide dinitrate approved for the treatment of heart failure in self-identified blacks. Although evidence exists that the mechanism of benefit of the agent may be related to the reduced production of nitric oxide in blacks, this is not established with certainty. Environmental influence cannot be completely ruled out. Similarly, it is unclear whether a genetic basis exists for the superior response to this drug combination by blacks than by whites. If a genetic basis does exist, can skin color serve as an adequate marker? The degree of racial intermixing that has occurred over the years calls into question the genetic significance of skin color. In fact, it is becoming increasingly difficult to judge the significance of manuscripts studying blacks or African Americans due to the increasing prevalence of multiracial individuals.

But I digress; it was the financial implications of BiDil that were being discussed. Hydralazine and isosorbide, of course, are old drugs that have long since gone off patent. Checking again with a local pharmacy, a 20-mg isosorbide pill costs $0.50 and either 25- or 50-mg tablets of hydralazine sell for approximately $0.80. In contrast, BiDil, which contains 37.5 mg hydralazine and 20 mg isosorbide, sells for about $2.36. Thus, BiDil is nearly twice as expensive as its individual components. Although the prices at the University of California at San Diego (UCSD) pharmacy are somewhat lower, the differences are comparable.

Drug combinations with variable pricing have also figured prominently in the marketing of statins. Atorvastatin and the calcium-channel blocker amlodipine have been combined into Caduet, which actually varies from $0.44 more to $0.20 less per pill as a 5/20 combination than the equivalent doses of individual pills. Vitorin, the marriage of the lipid-lowering agents simvastatin and ezetimibe, is actually much less expensive at $2.50 for a 10/20 pill than the $6.30 charged for the same doses separately. Competitive pricing may play a role in this, because an equivalent dose of atorvastatin and ezetimibe would be $5.40.

We are perhaps witnessing the epitome of combination drug marketing with the advent of the clinical trials of torcetrapib. This agent is a cholesterol ester transfer protein inhibitor that has been shown to have the potential to produce a 50% to 100% increase in high-density lipoprotein, a therapeutic target that has so far eluded us. However, the pivotal clinical trials, for which I am an investigator, are all examining the efficacy of the combination of torcetrapib and atorvastatin, and not the agent alone as an add-on to low-density lipoprotein-lowering therapy. Thus, evidence-based medicine will only have data for torcetrapib/atorvastatin to guide usage, and approval by the Food and Drug Administration will likely be limited to the combination preparation. The drug will likely be unavailable to those who cannot tolerate statins and will help sustain the price of atorvastatin even after it goes off patent. Many prior drug

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combinations have been implemented after approval and had advantages both in the scientific field and in the marketplace. Torcetrapib, however, represents the initial example of an agent whose research program is based on combined therapy, a factor that will have major implications in the pricing and selling of this drug as well as that of atorvastatin.

Let me issue a disclaimer and concede that I do not have an MBA nor am I experienced in the world of business. I am not very knowledgeable about issues such as unit cost and pricing or the expenses entailed in drug development, marketing, and advertising. Therefore, it is perhaps not surprising that I do not understand the various pricing schemes just presented. However, I find it inescapable that much of the approach to selling prescription drugs is similar to that applied to selling used cars, life insurance, Christmas trees, or most other commodities. It is clear that the pharmaceutical industry must be profitable to perform research and develop new drugs and that society has benefited enormously from its accomplishments. No one would want to hinder the innovative work of pharmaceutical companies in any way. However, the treatment of disease is not discretionary on the part of the patient, and the calling to cure disease and ease suffering has been afforded a high station by society. It would be a shame if that patina of nobility was tarnished by machinations in the marketplace, especially if such actions placed important medications beyond the financial reach of those who need them. I urge the pharmaceutical industry, and those agencies responsible to oversee it, to work to make the prices for prescription drugs as rational and cost effective as possible, and to ensure that new agents are evaluated to be applicable in the broadest possible clinical settings.

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